

Survival of non-surgical patients with mild angina or myocardial infarction without angina

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SUMMARY A group of 408 catheterised patients who had mild angina or myocardial infarction without angina was selected in conformity with the criteria for entry into a previously reported randomised trial. Medical treatment had been chosen initially by the cardiologist, referring physician, or the patient, although 27% had late operation. Five year survival rates were 91% and 72% for mild angina with high or low ejection fractions and 85% for those who had myocardial infarction without subsequent angina. Survival rates were 95%, 88%, and 80% for one, two, and three artery disease respectively. For patients who had ejection fractions of at least 0.50, five year survivals were 95%, 89%, and 83% for one, two, and three artery involvement respectively. Good left ventricular function, single artery disease, and a short history were favourable prognostic variables in multivariate analysis of patients who had angina pectoris. Statistical methods of dealing with patients who had late operation influenced calculated survival, especially for patients at relatively high risk. The lower survival rates for the whole group and most subsets compared with survival rates in the randomised trial may be of clinical importance.

The Coronary Artery Surgery Study included a randomised trial comparing a strategy of early elective operation with operation deferred contingent on worsening symptoms (medical group) in patients who had mild angina pectoris or myocardial infarction without subsequent angina.¹ The failure of the Coronary Artery Surgery Study trial to show a difference in survival between medical and surgical patients may be due to the high survival of the medical group, which was perhaps influenced by crossover from medical to surgical treatment because of worsening symptoms.¹ The Coronary Artery Surgery Study group also studied survival in randomisable but not randomised patients; the prognoses of most of the various subsets were similar to those of the randomised group.² This similarity suggests that other groups might usefully review their experience with similarly selected patients to determine the clinical reproducibility of the favourable prognosis of the medically treated group.

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Patients and methods

The objective was study of a group of patients whose inclusion criteria conform closely to those used by the Coronary Artery Surgery Study for randomisation in the clinical trial.³ The dates of catheterisation were confined to the 46 months (August 1975 to 31 May 1979) of selection of the Coronary Artery Surgery Study patients. There were certain intentional deviations from the Coronary Artery Surgery Study entry criteria.^{1,3} Although the basis for selection of Coronary Artery Surgery Study groups A and B (separated by the level of ejection fraction) was anginal pain that was particularly pronounced upon exertion, some patients had non-exertional pain.^{1,2} We decided to exclude patients who had non-exertional pain only or in association with exertional pain, because the criteria for non-exertional pain were not specified.^{1,3} Unstable angina was defined by the Coronary Artery Surgery Study as episodes of ischaemic pain that warranted emergency hospital admission for suspected or impending myocardial infarction.³ Because of difficulties in applying this definition we excluded all patients who had prolonged pain (exceeding 15 min)

or pain of increasing frequency in the two months before arteriography. Although unstable angina pectoris was an exclusion criterion in the Coronary Artery Surgery Study if it occurred in the two months before arteriography, myocardial infarction was not grounds for exclusion if it was encountered at least three weeks before arteriography. We decided to exclude patients who were otherwise qualified for inclusion in Coronary Artery Surgery Study groups A and B if myocardial infarction occurred within two months of arteriography, in order that exclusion for unstable angina and myocardial infarction might be uniform. Each of these three intentional deviations from Coronary Artery Surgery Study criteria for groups A and B might be expected to affect survival favourably. To sharpen the Coronary Artery Surgery Study criteria for group C (myocardial infarction without subsequent angina), only patients with electrocardiographic evidence of definite or questionable myocardial infarction accompanied by angiographic evidence of localised impairment of left ventricular contractility were considered for inclusion. In groups A and B myocardial infarction was diagnosed solely on the basis of abnormal Q or QS deflections that were considered to be diagnostic of myocardial infarction. Finally, because our experience indicated a relatively low survival for patients with 50–69% narrowing of the left main coronary artery, and because the Coronary Artery Surgery Study study included only a small number of such patients, we decided to exclude patients with this type of lesion.

Study was restricted to residents of the United States and Canada who were catheterised at the Cleveland Clinic Foundation for suspected coronary disease during the 46 months' Coronary Artery Surgery Study entry period. All patients under age 66 years whose records were coded in our computer registry as having angina pectoris class 1 or 2 or myocardial infarction without subsequent angina were considered to be eligible for study if they had been deemed to have 70% narrowing of at least one coronary artery and bypass surgery had not been performed within 90 days of arteriography. Valvar heart disease and cardiomyopathy were grounds for exclusion. During the 46 month entry period, 95% of surgical patients had bypass operation < 90 days after catheterisation. The clinical record of each of 1837 patients who satisfied these criteria was reviewed without knowledge of survival status. The modified Coronary Artery Surgery Study criteria were used for patient selection. Two hundred and ninety seven (of 1048) patients qualified for groups A and B and 111 (of 789) for group C as defined above. Our coding of functional class 2 was broader than that of the Canadian grading of angina used by

the Coronary Artery Surgery Study.^{3,4} Ability to walk 100 yards to $\frac{1}{4}$ mile (91–400 m) at a normal pace on level ground qualified for class 2 in our system, but the Canadian grade II requires the ability to walk more than two blocks (more than approximately 200 yards (182 m)) before pain. Therefore the Canadian grade II angina is milder than our class 2, and this difference was considered in the reclassification into the Coronary Artery Surgery Study-equivalent group. In fact the difference in coding angina was the most frequent reason for exclusion of 751 anginal patients who did not qualify. Severe arterial narrowing restricted to arteries supplying non-viable myocardium was the principal cause for exclusion in the group having myocardial infarction without subsequent angina.

Because of differences from the Coronary Artery Surgery Study in methods of coding, electrocardiograms of all patients were reviewed independently of any clinical or survival information and were recorded by the Minnesota criteria.⁵ The Coronary Artery Surgery Study coding used a modification of the Minnesota system; the exact nature of this was not reported.

Ejection fraction was not determined routinely at the time of catheterisation, although descriptions of ventricular contractility were coded in such a way that a score comparable to that used by the Coronary Artery Surgery Study could be determined.³ For this study the catheterisation films were reviewed and the ejection fraction was determined without knowledge of clinical data. Films of two patients with myocardial infarction but no angina had been lost in the post. Both had impairment of more than one ventricular segment and probably had ejection fraction < 0.50 but > 0.35. The ejection fraction was determined for the remaining 406 patients.

The follow up of patients was accomplished by a review of clinical records, written questionnaires, or telephone interviews with the patients, their families, or their physicians. Seven (1.7%) patients could not be located. Two patients were known to be living but their status is otherwise unknown.

The determination of the zero time for survival analyses conformed to the method used in the Coronary Artery Surgery Study randomisable study.² The interval between arteriography and bypass surgery was 90 days or less in 95% of patients who had both procedures at the Cleveland Clinic Foundation from August 1975 to 31 May 1979. The average interval between catheterisation and operation was 15.5 days for this group. Survival was counted from the seventeenth day after arteriography. No deaths occurred during the 16 day period after catheterisation in patients who were eligible for inclusion in the study.

All surviving patients were followed up for a minimum of 56 months and the mean follow up period for survivors was 80 months. One follow up was for 56 months, one for 57, one for 58, and nine for 59 months; all others were followed a minimum of five years.

Univariate survival analysis was done by standard life table methods.⁶ Except in one example (table 3)

all survival analyses were uncensored—patients were retained after coronary surgery was performed, as in the Coronary Artery Surgery Study. Survival curves were compared by use of the generalised Wilcoxon statistic.⁷ Significance levels of ≤ 0.05 were considered to be statistically significant. Multivariate analysis of survival was done by use of the Cox proportional hazards model.⁸

Table 1 Baseline clinical variables in study groups

Variable	A	B	C	All
Patients (No)	(271)	(26)	(111)	(408)
Age (yr):				
Mean	53.5	52.6	51.3	52.8
SD	7.4	7.0	7.3	7.4
Male	88.9	100.0	92.8	90.7
Angina (Canadian grading):				
None	0.0	0.0	100.0	27.2
I	15.1	15.4	0.0	11.0
II	84.9	84.6	0.0	61.8
Cigarette use:				
Present smoker	45.0	53.8	61.3	50.0
Non-smoker	51.7	42.3	34.2	46.3
Unknown	3.3	3.9	4.5	3.7
Reported history of:				
Hypertension	39.5	26.9	31.5	36.5
Previous MI	42.4	80.8	93.7	58.8
Heart disease in family	55.0	53.9	54.1	54.7
Congestive failure	1.5	3.9	4.5	2.5
Diabetes mellitus	7.8	23.1	7.2	8.6
Stroke	1.5	0.0	4.5	2.2
Peripheral artery disease	11.1	3.9	6.3	9.3
Medication at entry*:				
Nitrites (long acting)	55.8	61.5	42.3	52.4
Beta blocking	28.8	50.0	13.5	26.0
Digitalis	5.2	23.1	11.7	8.1
Antiarrhythmic	3.7	15.4	20.7	9.1
Anticoagulant	6.3	15.4	12.6	8.6
Dipyridamole	1.5	0.0	2.7	1.7
Thiazides	23.8	7.7	12.6	19.7
Other antihypertensives	13.0	15.4	10.8	12.6
Furosemide	2.2	3.8	2.7	2.5
Unknown diuretic	0.4	3.8	0.0	0.5
Lipid lowering	12.6	11.5	3.6	10.1
None of above	24.9	15.4	27.0	24.9
Systolic blood pressure:				
Average (mm Hg)	139	129	130	136
SD (mm Hg)	20	17	18	20
≥ 160 mm Hg (%)	17.0	7.7	9.9	14.5
Diastolic blood pressure:				
Average (mm Hg)	85	83	82	84
SD (mm Hg)	12	11	9	11
≥ 100 mm Hg (%)	13.3	3.9	7.2	11.0
ECG findings:				
Q wave MI (%)	29.5	76.9	100.0	51.7
? Q wave MI (%)	4.4	7.7	16.2	7.8
ST depression (%)	35.8	61.5	35.1	37.3
T wave inversion (%)	33.2	84.6	80.2	49.3
Conduction defect (%)	7.4	11.5	4.5	6.9
Any of the above (%)	62.4	100.0	100.0	75.0
Normal (none of the above)	37.6	0.0	0.0	25.0
Serum cholesterol:				
Patients (No)	(269)	(26)	(110)	(405)
Average (mg/dl)	268	268	260	266
SD (mg/dl)	58	50	54	56
≥ 250	59.1	57.7	56.4	58.3
Cardiothoracic ratio:				
Patients (No)	(268)	(26)	(110)	(404)
≥ 50 (%)	5.2	11.5	13.6	7.9

*Medication was not noted in two group A patients.

Conversion: traditional units to SI—cholesterol: $38.7 \text{ mg/dl} = 1 \text{ mmol/l}$.

MI, myocardial infarction.

Results

Tables 1 and 2 show the baseline data and results of invasive tests on the 408 selected patients. Certain additional information is pertinent. The patient population was 99.8% white. The mean interval between myocardial infarction and coronary arteriography in group C patients was 7.3 months and in 10 the interval was > 1 year. No patient had a ventricular score that exceeded 15.

Five year survival for the 401 patients that we followed was 88.5% and survival was 78.9% at eight years. Bypass surgery was done within five years in 19.6% and within eight years in 27.2%. Figure 1 shows survival by numbers of arteries narrowed by at least 70%. The survival differences are statistically significant ($p < 0.003$). Figure 2 shows survival by division into Coronary Artery Surgery Study group A (mild angina with ejection fraction > 0.50), group B (mild angina with ejection fraction < 0.50), and group C (myocardial infarction without angina). The survival curves are statistically different ($p < 0.0001$). Figure 3 shows the survival of group A patients by number of arteries affected. The differences are not significant ($p = 0.10$). The difference in survival for single vessel compared with multivessel disease in this subset, however, is significant ($p = 0.04$). Lesions of the proximal anterior descending artery showed no significant difference ($p = 0.13$).

Survival rates for all patients having ejection fraction ≥ 0.50 compared with ejection fraction < 0.50 were different ($p < 0.0001$). Five year survivals were

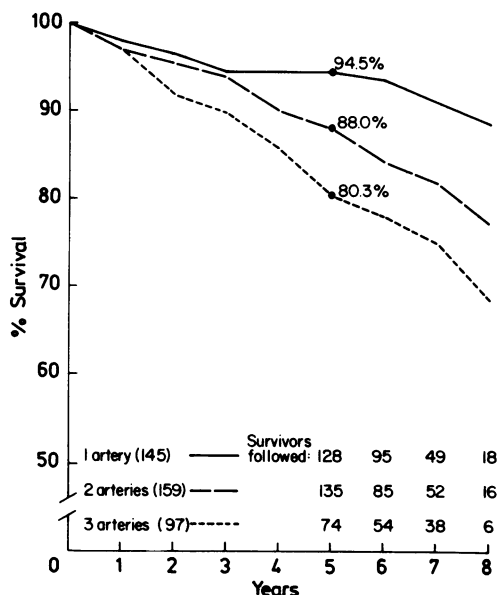


Fig 1 Survival by number of arteries affected. The numerals in parentheses indicate the numbers of patients at zero time; the other numerals refer to the numbers of survivors followed at five, six, seven, and eight years. Bypass surgery was done in 14%, 17%, and 32% of patients with one, two, and three artery disease respectively at five years, and 23%, 27%, and 32% at eight years ($p = 0.004$).

89.8% and 78.2%, respectively. Survivals were similar for group C patients with ejection fractions of ≥ 0.50 and ejection fractions of 0.35–0.49. Figure 4

Table 2 Arteriographic and ventriculographic variables

Variable	A	B	C	All
Affected arteries ($\geq 70\%$ diameter stenosis):				
One	41.7	15.4	27.0	36.0
Two	35.8	30.8	50.5	39.5
Three	22.5	53.9	22.5	24.5
Affected arteries ($\geq 50\%$ diameter stenosis):				
Single	27.7	11.5	17.1	23.8
Double	34.0	26.9	43.2	36.0
Triple	38.4	61.5	39.6	40.2
Proximal LAD disease: ($\geq 70\%$ narrowing)	23.6	30.8	10.8	20.6
Left ventricular score (3):				
Patients (No)	(271)	(26)	(111)	(408)
Mean	6.0	9.0	7.6	6.6
SD	1.5	2.1	1.6	1.8
5 (normal)	48.0	0.0	0.0	31.9
6–10 (slightly abnormal)	49.1	65.4	91.0	61.5
11–15 (abnormal)	3.0	34.6	9.0	6.6
Ejection fraction:				
Patients (No)	(271)	(26)	(109)	(406)
Mean (SD)	74 (9.8)	37 (9.5)	62 (13.1)	69 (14.5)
≥ 0.50	100.0	0.0	80.7	88.4
0.35–0.49	0.0	69.2	19.1	9.6
< 0.35	0.0	30.8	0.0	2.0

LAD, left anterior descending artery.

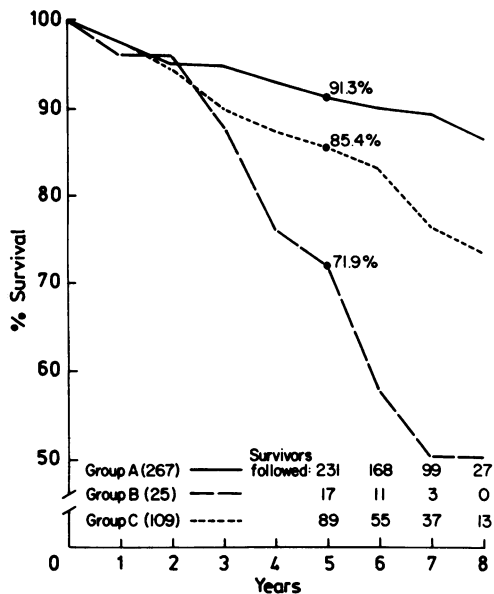


Fig 2 Survival by clinical group. Bypass surgery was done in 22% of both groups A and B and 14% of group C at five years, and 31%, 22%, and 17% of groups A, B, and C respectively at eight years.

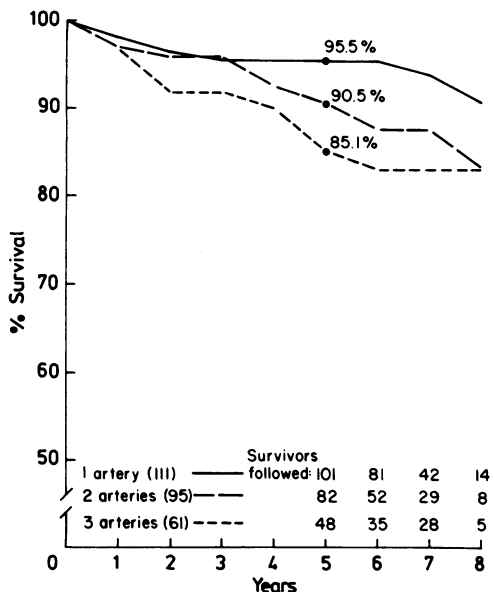


Fig 3 Survival in group A by number of arteries affected.

shows survival rates for patients with ejection fraction ≥ 0.50 by numbers of arteries affected. The differences are significant ($p < 0.02$). Only 46 patients had ejection fraction < 0.50 (five one artery disease, 20 two arteries, and 21 three arteries), so

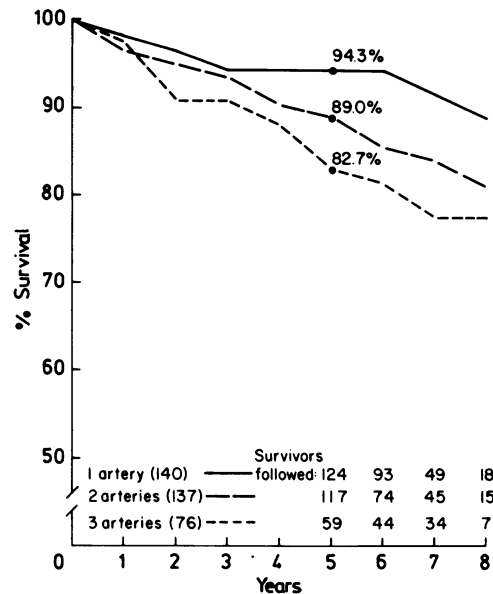


Fig 4 Survival in patients with ejection fraction ≥ 0.50 by number of arteries affected.

confidence in statistical analysis is low for these subsets, but no significant difference was demonstrated (five year survivals of 100%, 80%, and 71.4% for one, two, and three arteries, respectively). When Coronary Artery Surgery Study criteria for ventricular scoring were used as an index of ventricular function (fig 5), the differences in survival were significant ($p = 0.0004$).

Age < 50 years compared with ≥ 50 years did not influence survival ($p = 0.99$). The mean duration of symptoms in groups A and B was 40 months. Differences in survival related to this mean are significant ($p = 0.03$). Five year survival was 91.1% for those whose symptoms had been present for ≤ 40 months and 86.2% for the group with angina of longer duration. The survival curves of those with normal or abnormal electrocardiograms were not significantly different ($p = 0.07$). Survivals of the 44, 38, and 19 patients with normal electrocardiograms and one, two, and three artery disease respectively were not significantly different ($p = 0.44$). For the larger group with abnormal electrocardiograms, the differences were significant ($p = 0.003$). Five year survivals were 94.1%, 86.8%, and 78.1% for one, two, and three artery involvement respectively.

Both groups A and B had mild angina pectoris and could be analysed as a single group, though the two groups are distinct prognostically ($p < 0.0001$). The number of patients in group A greatly exceeds that in group B. Multivariate analysis of survival was

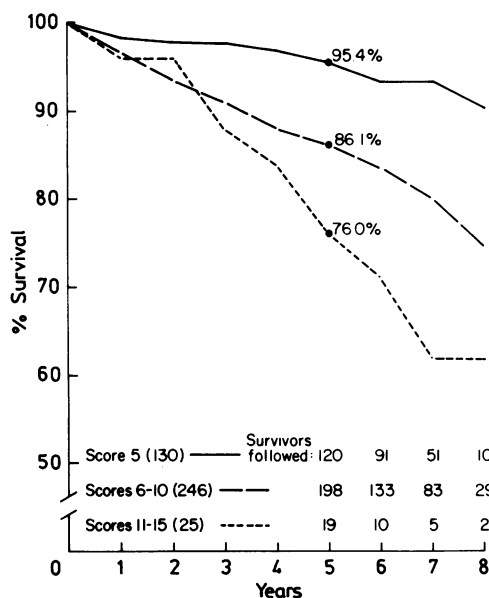


Fig 5 Ventricular score (Coronary Artery Surgery Study method).³ Score 5 means normal ventricle, scores 6-10 indicate mild impairment, and scores 11-15 represent moderate impairment.

done for groups A and B combined, for the following variables: age (years), ventricular score (5, 6-10, 11-15), electrocardiogram (normal or abnormal), number of arteries diseased, duration of symptoms (months), arteriosclerosis obliterans (yes or no), and hypertension or history of hypertension (yes or no). A ventricular score of 5 (normal ventricle) was the variable most predictive of survival. Compared with scores of >5, the difference in survival was significant ($p = 0.001$). Single artery disease also favoured survival when compared with multivessel involvement ($p = 0.009$). The duration of symptoms was the third variable, with the risk increasing 0.5% for every month increase in duration ($p = 0.06$). The other variables were not statistically significant.

Operation had not been advised by the cardiologist in many instances—29.2%, 19.2%, and 20.5% of groups A, B, and C respectively (26.2% for the whole group). Bypass surgery was performed within five years in 76 patients (19.0%) and in 92 (23.1%) during the entire follow up period. When survival analysis was done by considering patients as drop-outs at the date of operation lower rates than those calculated by retention of all patients in the study groups were found except for patients with disease of a single artery (table 3).

Failure of medical treatment (defined as death from cardiac cause, coronary surgery, or myocardial infarction) occurred within five years in 29.1%,

Table 3 Effect of censoring at the date of operation on percentage of five year survival

Group	Arteries	Censored (%)	Uncensored (%)
A		90.6	91.3
B		66.3	71.9
C		84.2	85.4
	1	95.5	94.5
	2	86.8	88.0
	3	72.2	80.3
A	1	97.1	95.5
A	2	89.1	90.5
A	3	77.0	85.1

Censored means that patient was dropped from survival analysis after crossover to surgery. Uncensored indicates that patients were retained for statistical analysis even though operation had been performed. This was the method used in Coronary Artery Surgery Study and European studies.^{1 10}

54.0%, and 33.6% of group A, B, and C patients respectively.

Discussion

The results of a randomised trial are best tested by repetition of the trial. For various reasons repetition may not be feasible, as in the case of the Coronary Artery Surgery Study randomised trial. Survival of Coronary Artery Surgery Study randomisable (eligible but not randomised) medically treated patients was similar to that of the randomised group despite considerable baseline differences.² A recent Coronary Artery Surgery Study report indicates that survival of registry patients having mild angina and ejection fractions >45% was similar to that of randomised patients.⁹ These observational studies were intended to demonstrate the clinical applicability of the results of the randomised prospective trial. Observational surveys cannot be compared confidently with randomised prospective investigations, even if adherence to entry criteria is rigid. Unrecognised or unreported differences in selection of patients and variations in treatment may create bias. The intent of the present survey is not a challenge of the validity of the reported randomised prospective trials, but to test the clinical reproducibility in an independent group of medically treated patients.

Medical and surgical treatment of coronary disease cannot be compared because of the high crossover from medical treatment to operation.^{1 10} The European Coronary Artery Study Group states that the policy of treatment is being studied, and the Coronary Artery Surgery Study compares early elective operation with operation deferred contingent on worsening symptoms. Because the intent to treat medically or surgically is being studied, all patients are required to remain in their assigned groups, regardless of subsequent treatment. This is

also true for the Coronary Artery Surgery Study randomisable study: after determination of the date at which early elective surgery closed, all other patients were considered to be medical cases and there was no statistical crossover to operation. The present study was designed to conform to the selection criteria of the Coronary Artery Surgery Study randomised study, and the last date of elective surgery was determined in a similar manner to that used in the Coronary Artery Surgery Study randomisable patients. The percentages of crossover to surgical treatment are little different in the Coronary Artery Surgery Study randomised and randomisable groups and the European study, and slightly lower in the present investigation.

Except for the five intentional deviations mentioned in the methods section, selection conformed to the 18 criteria for inclusion or exclusion outlined in the Coronary Artery Surgery Study protocol.³ Most of the five intentional deviations would be expected to improve survival. The baseline characteristics of the Coronary Artery Surgery Study randomised and randomisable patients were similar except that there was more β blockade treatment, more single artery disease, and less three artery disease in the randomisable patients than in the randomised group assigned to medical treatment.² The present study more closely resembles the randomisable patients as far as distribution of arterial disease is concerned, as would be expected. There was less single artery disease and more disease of two arteries than in the Coronary Artery Surgery Study randomisable patients. Because of selection for early operation, fewer patients had lesions of the proximal anterior descending artery than in the randomisable group. The most striking differences in baseline characteristics between the present study group and Coronary Artery Surgery Study randomised or randomisable medical patients are the lower percentage of β blockade treatment, the higher percentage of ST segment depression, and the lower prevalence of cardiac enlargement in the present study.² The ST segment difference is unexpected because similar criteria were used in both studies.⁵ Originally the Coronary Artery Surgery Study had reported a higher percentage (43%) of ST segment depression in the randomised medical group.³ It is probable that the final Coronary Artery Surgery Study criterion of ST segment depression was more restrictive than the original coding, so our reading by Minnesota criteria would not be comparable.

The survival of all subsets reported in the Coronary Artery Surgery Study is lower in almost all instances in the present study.^{1,2} Five year survival was slightly higher than in the Coronary Artery Surgery Study randomised patients with single

artery disease (94% *vs* 93%) and group C patients had slightly higher survival (85% *vs* 84%) than in the Coronary Artery Surgery Study randomisable group. Group B was so small in the present study that survival of subsets is difficult to evaluate.

The most important comparisons should be with Coronary Artery Surgery Study group A patients. The Coronary Artery Surgery Study reported 95% and 94% five year survivals for randomised and randomisable patients respectively in group A and a survival of 91% was found in the present study. The percentages of patients having single artery disease may have an important bearing on group survival, but these figures are not available for Coronary Artery Surgery Study group A patients. The Coronary Artery Surgery Study did report survivals by number of arteries involved for randomised patients with ejection fractions ≥ 0.50 . Some of these were group C patients, but inclusion of these would not be expected to reduce survival appreciably because five year survival was so high in this group. The European results and those of the present study may be compared with Coronary Artery Surgery Study randomised patients on the basis of multivessel disease with ejection fractions ≥ 0.50 (table 4). The European study group is larger because of exclusion of groups B and C patients and those with single artery disease, and there are differences in selection of patients. The Coronary Artery Surgery Study randomised patients had five year mortalities of 5%, 3%, and 6% for one, two, and three artery disease respectively, and 5% for the whole group with ejection fractions ≥ 0.50 .¹ This was in the same range as for Coronary Artery Surgery Study registry patients with no severe coronary artery disease (6%).¹² The European mortality figures and those of the present study are in the same range and several times higher than those of the Coronary Artery Surgery Study randomised patients.

The Coronary Artery Surgery Study reported important baseline variables that affected survival in registry patients.¹² Table 5 shows these variables, in order of importance as listed in the final Cox model, for the Coronary Artery Surgery Study randomised group, the Coronary Artery Surgery Study random-

Table 4 Comparison of five year mortalities of patients with ejection fraction ≥ 0.50

No of arteries	CASS ¹ (%)	European ¹¹ (%)	CCF (%)
Two	3 (99)	11.8 (188)	11.0 (137)
Three	6 (90)	17.6 (154)	17.3 (76)

Numbers in parentheses are patients in each subset. European trial used 50% narrowing of coronary arteries instead of 70%. CASS, Coronary Artery Surgery Study; CCF, present report.

Table 5 Baseline characteristics in order of prognostic importance (Cox model¹³): expressed in percentages

	CASS randomised ²	CASS randomisable ²	European ¹⁰	CCF
Ventricular score:				
(Mean)	(7.43)	(7.40)	NA*	(6.60)
5	39.0	41.6		31.9
6-10	43.9	42.7		61.5
11-15	15.3	13.5		6.6
> 15	1.8	2.2		0
Age	50.9	50.7	49.9	52.8
Ejection fraction:				
(Mean)	(60.3)	(60.3)	(64.6)	(69.0)
≥ 0.50	77.6	81.0	100	88.4
0.35-0.49	20.2	14.9	0	9.6
< 0.35	2.2	4.1	0	2.0
Arteries:†				
1	27.4	40.3	0	36.0
2	38.0	36.8	41	39.5
3	34.6	23.0	50	24.5
Left main artery	1.5	2.3	8	0
Cigarettes	40.8	34.8	43	50.0

*Abnormal wall motion in 53%.

†European results are based on at least 50% narrowing rather than 70%.

CASS, Coronary Artery Surgery Study; NA, not available.

isable patients, the European study, and the present investigation. Only the mean age and the higher frequency of smokers were adverse factors that were more common in the present study. These would not explain the lower survival than in the Coronary Artery Surgery Study groups. Other baseline variables of prognostic importance may have been missed in the Coronary Artery Surgery Study multivariate analysis, and these might account for some survival differences. An obvious explanation for lower survival in the present study is that these patients had inferior medical treatment. If we assume the validity of the untested hypothesis that medical treatment improves survival in chronic coronary disease, the possible influence of medical treatment cannot be evaluated because no standard treatment was recommended to patients in randomised trials or to our patients. The safety of deferring operation rests on the assumption that worsening symptoms herald a change in prognosis and that unexpected sudden death is uncommon. If these assumptions are sound, it is possible that the physicians in the present study were less adept at recognising changes in risk during treatment than those in the Coronary Artery Surgery Study group, so survival might be lower. This concept cannot be tested.

One of the problems of comparing studies of coronary bypass surgery is the difference in criteria for operability in various institutions. This applies less to randomised trials in which specific criteria are imposed, but in the Coronary Artery Surgery Study randomisable study and many other reports selection for operation varied considerably among participating institutions. Although all patients in the

present report satisfied Coronary Artery Surgery Study criteria for operability, many had not been advised to have surgery.

The original intent of the Coronary Artery Surgery Study randomised trial was to drop medical patients at the date of operation.³ This approach was abandoned later, but it was stated that the change in statistical treatment did not alter the results.¹ In the present studies survival was lower, except for single artery disease, when patients were dropped at the date of operation. This suggests that surgical treatment improves survival of some patients or that operation was done in a low risk group. No evidence was found for the latter possibility.

The baseline characteristics in the present study would be expected to conform more closely to those of Coronary Artery Surgery Study randomised or randomisable groups than with those of a group of patients with mild angina or myocardial infarction without angina selected from routine practice without meticulous attempt to adhere to Coronary Artery Surgery Study entry criteria. Therefore, one would expect the survival results in this study group to resemble more closely those of the Coronary Artery Surgery Study groups than the results of patients selected less formally. Still less can Coronary Artery Surgery Study results be applied to patients who have mild angina but have not had coronary arteriography.

Because it is difficult to account for the survival differences, similar observational studies from other institutions would be useful in determining clinical applicability. Such answers might come from prospective investigation of patients having no or mild

symptoms, though many of these are now subjected to angioplasty.

Addendum

Since the completion of this paper one additional death at 80 months in a group A patient with disease of two arteries has been reported through the National Death Index in Bethesda, Maryland.

References

- 1 CASS Principal Investigators and their Associates. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: survival data. *Circulation* 1983;68:939-50.
- 2 CASS Principal Investigators and their Associates. Coronary Artery Surgery Study (CASS): a randomized trial of coronary artery bypass surgery: comparability of entry characteristics and survival in randomized patients and nonrandomized patients meeting randomization criteria. *J Am Coll Cardiol* 1984;3:114-28.
- 3 Principal Investigators of CASS and their Associates. The National Heart, Lung, and Blood Institute Coronary Artery Surgery Study (CASS). *Circulation* 1981;63(suppl II):1-81.
- 4 Campeau L. Grading of angina pectoris. *Circulation* 1976;54:522-3.
- 5 Rose GA, Blackburn H. *Cardiovascular survey methods*. World Health Organization Monograph 1968; No 56. Geneva: World Health Organization.
- 6 Cutler SJ, Ederer F. Maximum utilization of the life-table method in analyzing survival. *J Chronic Dis* 1958;8:699-713.
- 7 Breslow NE. A generalized Kruskal-Wallis test for comparing K samples subject to unequal pattern of censorship. *Biometrika* 1970;57:579-94.
- 8 Cox DR. Regression models and life tables (with discussion). *J R Stat Soc (Series B)* 1972;34:187-220.
- 9 Kennedy JW, Davis KB, Ryan TJ, Gersh BJ, Fisher LD. Selection of patients for coronary arteriography based on five year CASS survival [Abstract]. *Circulation* 1985;72:III-385.
- 10 European Coronary Surgery Study Group. Prospective randomized study of coronary artery bypass surgery in stable angina pectoris: a progress report on survival. *Circulation* 1982;Part II,65:67-71.
- 11 European Coronary Surgery Study Group. Long-term results of prospective randomized study of coronary artery bypass surgery in stable angina pectoris. *Lancet* 1982;ii:1173-80.
- 12 Ringqvist I, Fisher LD, Mock M, et al. Prognostic value of angiographic indices of coronary artery disease from the Coronary Artery Surgery Study (CASS). *J Clin Invest* 1983;71:1854-66.
- 13 Mock MB, Fisher L, Killip T, et al. The natural history of non-operated patients with ischemic heart disease: the CASS experience. In: Hammermeister KE, ed. *Coronary bypass surgery*. New York: Praeger, 1983:83-96.